IS AGGRESSIVE LOWERING OF BP IN ACUTE INTRACEREBRAL HAEMORRHAGE (ICH) BENEFICIAL: YES

Thorsten Steiner
Departments of Neurology, Klinikum Frankfurt Höchst and Heidelberg University Hospital, Germany

Thirty percent of patients with spontaneous acute intracerebral haemorrhage (ICH) suffer from hematoma expansion within 4 hours.[1-3] Increased blood pressure was identified as being one major risk factor of hematoma expansion.[4] On the other hand, reduction of blood pressure might lead to ischemia particularly adjacent to the haemorrhage. But, small positron emission tomography (PET) studies on the relation between cerebral blood flow (CBF) and blood pressure reduction could not prove ischemia in the peri-haematomal tissue.[5, 6] Also, a study on mitochondrial function in the peri-hematomal tissue from patients who were treated by an hematoma evacuation after an acute ICH did not demonstrate ischemia.[7]

Three randomized controlled trials (RCT) demonstrated that acute lowering of blood pressure was feasible and safe.[4, 8, 9] The Antihypertensive Treatment of Acute Cerebral Hemorrhage (ATACH) study used a "dose-escalating" design in 60 patients with acute ICH.[8] The study proved that keeping blood pressure within 3 systolic blood pressure targets (cohort 1: 170 to 200 mm Hg; cohort 2: 140 to 170 mmHg; cohort 3: 110 to 140 mm Hg) was feasible and safe. The Intensive blood pressure reduction in acute cerebral haemorrhage trial (INTERACT) study included 400 patients with acute ICH:[4] Patients were either treated by an intensive lowering of blood pressure below 140mmHg or by a standard guideline-based management of blood pressure below 180mmHg. It turned out that decreasing systolic blood pressure below 140mmHg lead to significantly smaller mean proportional haematoma growth. The INTERACT-2 used a similar design as the INTERACT study and looked at clinical efficacy of intensive blood pressure management within 6 hours after onset of ICH.[9] The primary endpoint (death or major disability, measured by modified Rankin Score (mRS) of 3 to 6) was observed in 52.0% receiving intensive treatment, and in 55.6% of patient receiving guideline-recommended treatment (OR, 0,87; 95% [CI], 0,75 to 1,01; P=0,06). The ordinal analysis demonstrated significantly lower modified Rankin Scores in the intensive treatment group (OR 0,87; 95% CI, 0,77 to 1,00; P=0,04). No differences were found for mortality and non-fatal serious adverse events at day 90. Subgroup analyses of INTERACT-2 consistently demonstrated trends favouring treatment with intensive lowering of blood pressure below 140 mmHg. Based on these results the European Stroke Organization (ESO) provided the following recommendation: "In acute ICH within 6 hours of onset, intensive blood pressure reduction (systolic target <140 mmHg in <1 hour) is safe and may be superior to a systolic target <180 mmHg. No specific agent can be recommended".[10]

Currently, the ATACH-2 trial is recruiting patients with spontaneous ICH to compare the effect of lowering blood pressure over 24 hours after onset below 180 mmHg or 140mmHg. The primary outcome is death or disability at three months.[11] Thus, ATACH-2 is looking at a clinical endpoint as it was done in INTERACT-2. The main differences between these two trials are: the shorter time window of 4,5 hours until treatment needs be established in ATACH-2 and the use of intravenous nicardipine as the only antihypertensive drug.

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